Complete Summary

GUIDELINE TITLE

Unresected stage III non-small cell lung cancer.

BIBLIOGRAPHIC SOURCE(S)

Lung Cancer Disease Site Group. Unresected stage III non-small cell lung cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Jan [online update]. 22 p. (Practice guideline; no. 7-3). [52 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Unresected, stage III non-small cell lung cancer (NSCLC)

Note: Unresected stage III non-small cell lung cancer is defined as: tumors which, for either technical or medical reasons, cannot be completely resected; either clinical or pathological stage III non-small cell lung cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Internal Medicine
Oncology
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To address the following questions:

- What is the role of different schedules or doses of radiotherapy in patients with unresected, clinical or pathological stage III non-small cell lung cancer (NSCLC)?
- Does chemotherapy combined with radiation therapy improve survival compared with radiation therapy alone in patients with unresected non-small cell lung cancer?

TARGET POPULATION

Adult patients with unresected, clinical or pathological stage III non-small cell lung cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Combination of chemotherapy (cisplatin-based and other types of chemotherapy) and radical radiotherapy
2. Hyperfractionated radiation alone (not recommended outside of clinical trial)
3. Variable dosing and scheduling of radiotherapy

MAJOR OUTCOMES CONSIDERED

Survival

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

1997 Guideline

MEDLINE and CANCERLIT searches were done for the years 1980 to June 1996. Search terms included: "NSCLC," "unresectable," "inoperable," "drug therapy," "radiotherapy," "clinical trials," "random allocation," "double-blind method," "guideline," and "meta-analysis." Articles identified by the searches, those cited in relevant papers and recently published reviews were retrieved and reviewed. Feedback on the Evidence-Based Recommendation report from practitioners in the province of Ontario and from one external reviewer also yielded information about

recent publications relevant to this guideline. These publications were reviewed and where appropriate, incorporated into this practice guideline.

2003 Update
The original literature search has been updated using MEDLINE (through December 2002), CANCERLIT (through October 2002), the Cochrane Library (Issue 4, 2002), and the proceedings of the annual meetings of the American Society of Clinical Oncology (1999 through 2002) and the American Society for Therapeutic Radiology and Oncology (1999 through 2002).

Inclusion Criteria
Articles were selected for inclusion in the systematic review of the evidence if they were full reports or abstracts of randomized controlled trials or meta-analyses that compared either (a) different radiotherapy schedules or doses or (b) radiotherapy versus combined modality therapy.

NUMBER OF SOURCE DOCUMENTS

1997 Guideline
14 source documents:

- One meta-analysis
- Nine randomized controlled trials
- Four randomized controlled trials published in abstract form

2003 Update
The following were found as of April 2000 and are incorporated into this version of the guideline:

- Two meta-analyses
- Four randomized controlled trials (one had been published in abstract form when reviewed for the original guideline)
- One practice guideline
- One economic analysis

Additional literature identified during updating activities between May 2000 and December 2002 will be incorporated into a re-written guideline:

- Twenty-four randomized controlled trials (five in abstract form, one updating a trial included in the meta-analyses)

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

1997 Guideline
There was no discussion of data pooling in the original document, and no data pooling was performed.

2003 Update
The information above remains current.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A key issue discussed by the Lung Cancer Disease Site Group (DSG) was the understanding that the available evidence on this topic is generalizable only to patients who have good performance status and minimal weight loss. It was agreed that the recommendation statement should reflect the fact that the results may not be generalizable to those patients with poor performance status and significant weight loss.

A second issue discussed by the Lung Cancer Disease Site Group was the lack of a threshold dose, regimen, or schedule for either chemotherapy or radiation therapy. The optimum method of integrating chemotherapy with radiotherapy is still under investigation. Dosing and scheduling issues are complex when using combined modality treatment, and treatment planning needs careful attention. While evidence can be found to support any one of several schedules for chemotherapy, it is up to individual clinicians to choose which is appropriate on a case-by-case basis.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 110 practitioners in Ontario (44 medical oncologists/hematologists, 16 radiation oncologists, 18 surgeons, and 32 respirologists/internists). The survey consisted of items evaluating the methods, results and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Lung Disease Site Group reviewed the results of the survey.

The guidelines were approved by the Lung Disease Site Group and the Practice Guideline Coordinating Committee. The original practice guideline was also reviewed by two external reviewers prior to publication in the journal Cancer Prevention and Control.

Update

The new information from review and updating activities was not subject to external review because it was consistent with the data used to inform the original practice guideline report.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note: The recommendations have not been modified since the original guideline was developed.

The Lung Cancer Disease Site Group is rewriting the practice guideline report and may revise the recommendations. The rewritten guideline report will include new evidence on the use of palliative radiotherapy, hyperfractionated radiotherapy, and accelerated radiotherapy in the treatment of unresected stage III disease, as well as evidence on the sequencing of chemotherapy relative to radiotherapy in combined modality regimens. When completed, the new practice guideline report will replace the current report.

Patients with good performance status (Eastern Cooperative Oncology Group [ECOG] 0 to 1) and minimal weight loss (less than 5% in the preceding three months) have been shown to have a survival benefit from treatment with combined chemo-radiotherapy and should be considered for this type of treatment approach. For these selected patients, thoracic irradiation of 60 Gy in 30 fractions over a six-week period in combination with cisplatin-based chemotherapy is recommended as a treatment option. A full discussion should occur between the patient and physician concerning the benefits, limitations, and toxicities of therapy.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

1997 Guideline

The following were eligible for inclusion in the systematic review of the evidence: one meta-analysis comprising 52 randomized controlled trials, with an analysis of individual patient data on 3,033 patients from 22 trials comparing combined chemotherapy plus radiotherapy versus radiotherapy alone; four randomized controlled trials of radiotherapy alone; one fully published randomized controlled trial of combined chemo-radiotherapy that was not included in the meta-analysis; four randomized controlled trials of hyperfractionated radiotherapy; and four randomized controlled trials published in abstract form of combined chemo-and radiotherapy in patients with unresected stage III non-small cell lung cancer.

2003 Update

The following were found through literature updating activities as of April 2000 and are incorporated into the current version of the guideline: two meta-analyses and full reports of three randomized controlled trials that compared radiotherapy alone with combined modality therapy (one of the randomized controlled trials was the full report of a trial included in the original practice guideline report which had been reported in abstract form only); one randomized controlled trial which compared concurrent versus sequential administration of radiotherapy with chemotherapy; one practice guideline; and one economic analysis.

Additional literature identified during updating activities between May 2000 and December 2002 will be incorporated into the re-written guideline and includes the following: nine randomized controlled trials of radiotherapy alone; six randomized controlled trials which compared radiotherapy alone with combined modality therapy (including one abstract report, and one report updating a trial included in the meta-analyses); four randomized controlled trials involving hyperfractionated radiotherapy; one randomized trial involving accelerated radiotherapy; and four trials (reported in abstract form) that compared different sequences of chemotherapy/radiotherapy administration.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- One meta-analysis detected a statistically significant overall benefit at two years for the use of combined chemo- and radiotherapy compared with radiotherapy alone. A hazard ratio of 0.90 (95% confidence interval, 0.83 to 0.97) or a 10% reduction in the risk of death translated into an absolute benefit of 3% at two years and 2% at five years. Subgroup analysis comparing combined chemo- and radiotherapy with cisplatin-containing regimens versus radiotherapy alone demonstrated a 13% reduction in the risk of death in the combined treatment arm (pooled hazard ratio, 0.87; 95% confidence interval, 0.79 to 0.96). This represents an absolute benefit of 4% at 2 years.
- A second meta-analysis detected a statistically significant advantage to cisplatin-based combination chemotherapy compared with chemotherapy

alone. In the cisplatin-based combination chemotherapy group, the reduction in mortality at one and two years was 24% and 30%, with an odds ratio for death of 0.76 (95% confidence interval, 0.6 to 0.9) at one year and 0.70 (95% confidence interval, 0.5 to 0.9) at two years. A third meta-analysis showed a statistically significant advantage to combined modality therapy over radiotherapy alone. The overall relative risk of death for combined modality therapy was 0.87 (95% confidence interval, 0.81 to 0.94; 13% reduction in relative risk) at two years and 0.83 (95% confidence interval, 0.77 to 0.90; 17% reduction in relative risk) at three years, in favour of combined chemo-radiotherapy.

- Patients with good performance status (Eastern Cooperative Oncology Group [ECOG] 0 to 1) and minimal weight loss (less than 5% in the preceding three months) have been shown to have a survival benefit from treatment with combined chemo-radiotherapy and should be considered for this type of treatment approach.

POTENTIAL HARMS

Toxicity from chemotherapy and/or radiotherapy is largely confined to neutropenic-related infection, weight loss and vomiting. Serious infections requiring hospitalization and weight loss are more prevalent in combined modality therapy (sequential chemo-radiotherapy) compared to radiation alone. Patients receiving concurrent combined chemo-radiotherapy may also be at risk for radiation pneumonitis and esophagitis.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Patients not fitting the criteria mentioned in the major recommendations section are not candidates for combined modality treatment. Those experiencing symptoms amenable to treatment should receive palliative thoracic irradiation.
- At this time, hyperfractionated radiation is not recommended outside the context of a clinical trial.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Lung Cancer Disease Site Group. Unresected stage III non-small cell lung cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Jan [online update]. 22 p. (Practice guideline; no. 7-3). [52 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1997 Mar 14 (updated online 2003 Jan)

GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

The Provincial Lung Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Lung Cancer Disease Site Group disclosed potential conflict of interest information.

GUIDELINE STATUS

This is the current release of the guideline.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Unresected stage III non-small cell lung cancer. Summary. Toronto (ON): Cancer Care Ontario. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 5, 1999. The information was verified by the guideline developer as of February 22, 1999. This NGC summary was updated by ECRI on December 17, 2001 and most recently on July 21, 2003. The most recent information was verified by the guideline developer as of August 6, 2003.

COPYRIGHT STATEMENT

Date Modified: 11/15/2004


FIRSTGOV